

1. (amended) A method for identifying a compound that modulates a heat shock protein (HSP)-alpha (2) macroglobulin ( $\alpha$ 2M) receptor-mediated process, comprising:

- (a) contacting a test compound with: (i) an isolated alpha (2) macroglobulin receptor, or a ligand-binding fragment thereof; and (ii) a purified heat shock protein, or a binding fragment thereof, or a purified HSP-peptide complex; and
- (b) measuring the level of alpha (2) macroglobulin receptor activity or expression,

*B<sup>1</sup>* such that if the level of activity or expression measured in (b) differs from the level of alpha (2) macroglobulin ~~receptor activity~~ in the absence of the test compound, then a compound that modulates an HSP- $\alpha$ 2M receptor-mediated process is identified.

2. (amended) The method of claim 1, in which the compound identified is an antagonist which interferes with an HSP- $\alpha$ 2M receptor-mediated process.

*B<sup>2</sup>* 11. (amended) The method of claim 1, in which the compound is an agonist which enhances an HSP- $\alpha$ 2M receptor-mediated process.

13. (amended) A method for identifying a compound that modulates an HSP- $\alpha$ 2M receptor-mediated process, comprising:

- (a) contacting a test compound with: (i) an alpha (2) macroglobulin receptor- or ligand binding fragment- expressing cell; and (ii) a purified heat shock protein, or fragment thereof, or a purified HSP-peptide complex; and
- (b) measuring the level of alpha (2) macroglobulin receptor binding activity in the cell,

*B<sup>3</sup>* such that if the level of alpha (2) macroglobulin receptor binding activity measured in (b) differs from the level of alpha (2) macroglobulin receptor binding activity in the absence of the test compound, then a compound that modulates an HSP- $\alpha$ 2M receptor-mediated process is identified.

14. (amended) The method of claim 1 or 13 wherein the alpha (2) macroglobulin receptor activity measured is the ability to bind to a heat shock protein.

17. (amended) The method of claim 1 or 13 wherein the alpha (2) macroglobulin receptor activity measured is the ability to bind to a heat shock protein, wherein measuring the level of alpha (2) macroglobulin receptor activity of step (b) comprises measuring the amount of heat shock protein, or binding fragment thereof, bound to the alpha (2) macroglobulin receptor, or ligand-binding fragment thereof, such that if the amount of bound heat shock protein measured in (b) differs from the amount of bound heat shock protein measured in the absence of the test compound, then a compound that modulates the binding of an HSP to the  $\alpha$ 2M receptor is identified.

B4 18. (amended) The method of claim 1 or 14, in which the alpha (2) macroglobulin receptor contacted in step (a) is on a cell surface.

19. (amended) The method of claim 1 or 14, wherein the alpha (2) macroglobulin receptor is immobilized to a solid surface.

21. (amended) The method of claim 14 wherein the amount of bound heat shock protein is measured by contacting the cell with a heat shock protein-specific antibody.

B5 22. (amended) The method of claim 14 wherein the heat shock protein is labeled and the amount of bound heat shock protein is measured by detecting the label.

Add new claims 64-76 as follows:

64. (new) The method of claim 1 or 13, wherein the alpha (2) macroglobulin receptor is purified.

B6 65. (new) The method of claim 1 or 13, wherein the expression measured is alpha (2) macroglobulin receptor gene expression.

66. (new) The method of claim 1 or 13, wherein the expression measured is alpha (2) macroglobulin receptor gene product expression.


67. (new) The method of claim 14, wherein the derivative, analog, fragment, or domain of the alpha (2) macroglobulin receptor is purified.

68. (new) A method for identifying a compound that modulates an HSP- $\alpha$ 2M receptor-mediated process, comprising:

- (a) contacting a test compound with an alpha (2) macroglobulin receptor-expressing cell and a purified heat shock protein, or fragment thereof, or a purified HSP-peptide complex; and
- (b) measuring the level of alpha (2) macroglobulin receptor activity by a signal transduction activity assay, heat shock protein uptake assay, chemotaxis assay, or calcium ion concentration assays,

such that if the level of alpha (2) macroglobulin receptor activity measured in (b) differs from the level of alpha (2) macroglobulin receptor activity in the absence of the test compound, then a compound that modulates an HSP- $\alpha$ 2M {receptor-mediated process} is identified.

69. (new) A method for screening a plurality of molecules for one or more molecules having the ability to modulate, directly or indirectly, the antigen presentation activity of alpha (2) macroglobulin receptor-expressing cells, comprising:

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- (a) contacting said plurality of molecules with the alpha (2) macroglobulin receptor-expressing cells and a purified complex of a heat shock protein and the antigenic peptide;
  - (b) measuring antigen presentation by said alpha (2) macroglobulin receptor-expressing cells in the presence of said plurality of molecules; and
  - (c) comparing antigen presentation activity by said alpha (2) macroglobulin receptor-expressing cells in the presence of said plurality of molecules with antigen presentation activity by said alpha (2) macroglobulin receptor-expressing cells in the absence of said plurality of molecules

wherein a lower or higher degree of antigen presentation indicates that one or more molecule(s) modulates the antigen presentation activity by said alpha (2) macroglobulin receptor-expressing cells.

70. (new) A method for screening an antibody specific to a heat shock protein or an alpha (2) macroglobulin receptor for the ability to modulate, directly or indirectly, the antigen presentation activity of alpha (2) macroglobulin receptor-expressing cells, comprising:

- (a) contacting said antibody with the alpha (2) macroglobulin receptor-expressing cells and a purified complex of a heat shock protein and the antigenic peptide;
- (b) measuring antigen presentation by the alpha (2) macroglobulin receptor-expressing cells in the presence of said antibody; and
- (c) comparing antigen presentation activity by the alpha (2) macroglobulin receptor-expressing cells in the presence of said antibody with antigen presentation activity by the alpha (2) macroglobulin receptor-expressing cells in the absence of said antibody,

wherein a lower or higher degree of antigen presentation indicates that said antibody modulates the antigen presentation activity by the alpha (2) macroglobulin receptor-expressing cells.

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71. (new) A method for screening a molecule for the ability to modulate, directly or indirectly, the antigen presentation activity of alpha (2) macroglobulin receptor-expressing cells, comprising:

- (a) contacting said molecule with purified alpha (2) macroglobulin receptor-expressing cells and a purified complex of a heat shock protein and an antigenic peptide;
- (b) measuring antigen presentation by the alpha (2) macroglobulin receptor-expressing cells in the presence of said molecule; and
- (c) comparing antigen presentation activity by the alpha (2) macroglobulin receptor-expressing cells in the presence of said molecule with antigen presentation activity by the alpha (2) macroglobulin receptor-expressing cells in the absence of said molecule,


wherein a lower or higher degree of antigen presentation indicates that said molecule modulates the antigen presentation activity by said alpha (2) macroglobulin receptor-expressing cells.

72. (new) A method for screening a plurality of molecules for one or more molecules having the ability to modulate, directly or indirectly, activation of cytotoxic T cells against a peptide *in vitro* by an alpha (2) macroglobulin receptor-expressing cell, comprising:

- (a) contacting said plurality of molecules with: (i) cells expressing alpha (2) macroglobulin receptor; (ii) a purified complex of a heat shock protein and a peptide; and (iii) cytotoxic T cells, under conditions conducive to the activation of cytotoxic T cells;
- (b) comparing the activation *in vitro* of said T cells with the activation *in vitro* of T cells in the absence of said plurality of molecules,

wherein a lower or higher degree of T cell activation indicates that one or more molecules in said plurality of molecules modulates the ability of the alpha (2) macroglobulin expressing cells to stimulate the activation of cytotoxic T cells against the peptide.

73. (new) A method for screening an antibody specific to a heat shock protein or an alpha (2) macroglobulin receptor for the ability to modulate, directly or indirectly, activation of cytotoxic T cells against a peptide *in vitro* by an alpha (2) macroglobulin receptor-expressing cell, comprising:

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- (a) contacting the antibody with: (i) cells expressing alpha (2) macroglobulin receptor; (ii) a purified complex of a heat shock protein and a peptide; and (iii) cytotoxic T cells, under conditions conducive to the activation of cytotoxic T cells;
  - (b) comparing the activation *in vitro* of said T cells with the activation *in vitro* of T cells in the absence of said plurality of molecules,

wherein a lower or higher degree of T cell activation indicates that the antibody modulates the ability of the alpha (2) macroglobulin -expressing cells to stimulate the activation of cytotoxic T cells against the peptide.

74. (new) A method for screening a molecule for the ability to modulate, directly or indirectly, activation of cytotoxic T cells against a peptide *in vitro* by an alpha (2) macroglobulin receptor-expressing cell, comprising:

- (a) contacting said molecule with: (i) purified cells expressing alpha (2) macroglobulin receptor; (ii) a purified complex of a heat shock protein and a